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Synthesis and anti-microbial activity of novel series of *N*-(substituted phenyl-*1H*-tetrazol-1-yl)-7-substituted tetrazolo [1,5-a]quinoxalin-4yl-amine derivatives

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ABSTRACT

*In recent years, tetrazoles fused with quinoxaline ring have been grabbing the attention of the synthetic chemists for their pharmacological and medicinal applications. In the present work, we describe the novel series of derivatives of N-(Substituted phenyl-1H-tetrazol-1-yl)-7-substituted tetrazolo[1,5-a]quinoxalin-4-amine were synthesized by treating the 4-[(2E/Z)-substituted benzylidenehydrazinyl]-7-substituted tetrazolo [1,5-a] quinoxaline with Sodium azide in methanol at 60-80^{o}C.The resulted compounds were characterized based on the bases of their spectral ^{1}H NMR, ^{13}C NMR, Mass, IR analyses. In vitro, most of the synthesized derivatives were screened for their anti-microbial activity against Gram positive bacteria S.aures and Gram negative bacteria E.Coli and anti-fungal activity carried out on C.albicans, A. niger. Compounds **4g, 4h, 4q** and **4n**, **4l** shows good activity against bacterial strains and **4g, 4h, 4r** and **4l** shows a moderate activity against fungal strains.*

Key words: Substituted 4-hydrazinyl tetrazolo*[1,5-a]*-quinoxaline, Substituted aromatic aldehydes, Sodium azide, Anti-microbial activity

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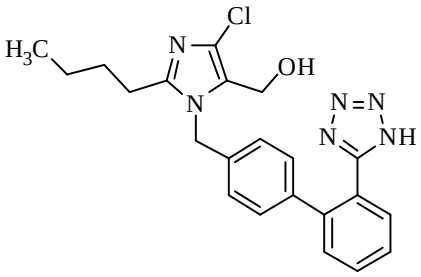
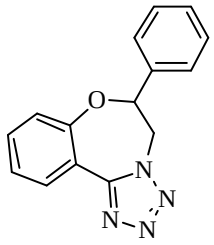
INTRODUCTION

Tetrazole and its derivatives are used for biological activities such as anti-bacterial, anti-inflammatory, anti-fungal, anti-viral, anti-tuberculosis, cyclooxy- genase inhibitors, antinociceptive, hypoglycemic and anticancer activities. A well-known tetrazole is MTT, which is dimethylthiazolyldiphenyltetrazolium salt which was used in MTT assay to quantify the respiratory activity of live cells in cell culture, although it kills cells in the process[1, 2]. Tetrazoles are also used as plant growth regulators, herbicides, and fungicides.[3] Tetrazole derivatives have potential for drug development for HIV or other immune diseases.[4,5] Additionally they have also application in photography [6] and specialty explosives.[7] They are resistant to metabolic degradation as well as to chemical oxidants.[8] A few examples which are used as drugs they are Losartan (**1V-2**) is an angiotensin-II antagonist and commonly used for treatment of hypertension, the compound 6-phenyl-5,6-dihydrotetrazolo[1,5-*d*][1,4]-benzoxazepine**(IV-3)** has also been found to posses binding affinity to benzodiazepine receptors.[9]



III-2



III-3

Moreover fusion of tetrazoles, which is considered as planar acidic heterocyclic analogue of carboxylic function [10,11] has the ability to increase potency [12,13] and improve bioavailability[14]. Similarly Schiff's bases of tetrazolo quinoxalines have been reported to exhibit anti-microbial activity.

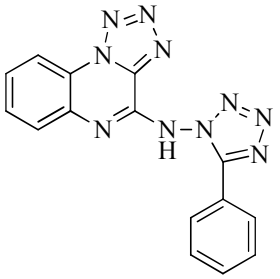
MATERIALS AND METHODS

Melting points were determined by the capillary tube method, and the thermometer was uncorrected. The progress of reaction was monitored by thin layer chromatography on silica gel plates. Elemental analysis was measured by using of Perkin Elmer 2400 CHN elemental analyzer. ^{1}HNMR were recorded on a Brucker WM-400MHz using TMS as an internal slandered, samples was dissolved in DMSO-$d_{6.}$ FT-IR Spectra were obtained as KBr discs on Perkin Elmer FT-IR240-Spectrometer. ^{13}CNMR spectra were recorded on a Brucker WM-100MHz using DMSO-$d_{6.}$ Mass spectra were recorded on a JEOL.SX-102 [ESI-MS]. The synthetic route for *N*-(substituted phenyl-*1H*-tetrazol-1-yl)-7-substituted tetrazolo *[1,5-a]*quinoxalin-4yl-amine described in **Scheme-1.**

General procedure for the synthesis of 4-[(2*E*)-Substituted benzylidene hydra-zinyl]-7-substituted tetrazolo*[1,5-a]* quinoxaline 3(a-p):
A mixture of substituted-4-hydrazinyltetrazolo*[1,5-a]*quinoxaline (0.01mol) **1(a-d)** and substituted aromatic aldehydes **2(a-e)** (0.01mol) in methanol (20mL) and dimethyl formamide (5mL) were refluxed for 3-4 h. The progress of reaction was monitored by TLC. After completion of the reaction, the reaction mass was cooled to room temperature, poured onto crushed ice, the solid separated, filtered and washed with methanol (20mL). The crude solid was purified by re-crystallization with ethanol.

General procedure for the synthesis of *N*-(substituted phenyl-*1H*-tetrazol-1-yl)-7-substituted tetrazolo *[1,5-a]*quinoxalin-4yl-amine 4(a-p):
A mixture of Substituted benzylidenehydrazinyl-7-substituted tetrazolo*[1,5-a]* quinoxaline **3(a-t)** (0.01mol) and sodium azide (0.02 mol) in ethanol (10mL) were refluxed for 3-4 h (the progress of the reaction was monitored by TLC), after completion of the reaction, it was cooled to room temperature, poured onto crushed ice, solid separated filtered, washed with water and re-crystallized with chloroform.

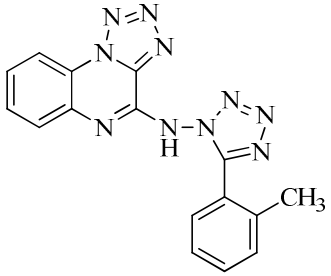
***N*-(5-phenyl-*1H*-tetrazol-1-yl)tetrazolo*[1,5-a]*quinoxalin-4yl-amine (4a):**



Yield: 67%; m.p:287-289 ^{o}C; IR (KBr, cm^{-1}): 1583 (C-N), 1643 (C=N), 3405 (-NH); ^{1}HNMR (400MHz, DMSO-d_6, δ ppm): δ 8.02-8.10 (m, 3H,Ar-H), 8.11-8.18 (m, 2H, Ar-H), 8.20-8.22 (dd, 2H, Ar-H), 8.23-8.30 (dd, 2H, Ar-H), 11.25 (br, s, 1H, -NH); ^{13}CNMR (100 MHz, DMSO-$d_{6,}$ δ ppm): δ 125.2, 125.6, 125.7, 126.6, 127.8, 128.3, 128.4,

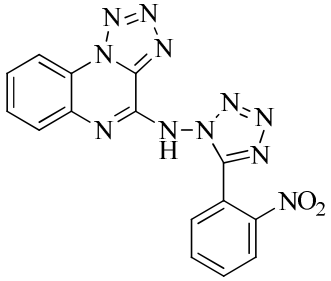
129.1, 129.5, 130.6, 135.2, 135.3, 142.5, 156.6, 161.2; MS (m/z): 331(M+H); Anal. Calcd for $C_{15}H_{10}N_{10}$: C: 54.54.; H: 3.05.; N: 42.41: Found: C: 54.49.; H: 3.01.; N: 42.38.

***N*-[5-(2-methylphenyl)-1*H*-tetrazol-1-yl]tetrazolo*[1,5-a]*quinoxalin-4yl-amine(4b):**



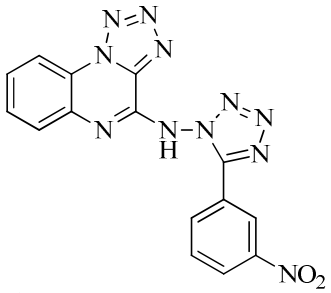
Yield: 69%; m.p:253-255 ^oC; IR (KBr, cm^{-1}): 1504 (C-N), 1641 (C=N), 3405 (-NH); ^{1}HNMR (400MHz, DMSO-d_6, δ ppm): δ 2.24 (s, 3H, -CH_3), 7.18-7.22 (m, 4H, Ar-H), 7.60-7.80 (m, 4H, Ar-H), 11.40 (br, s, 1H, -NH); ^{13}CNMR (100MHz, DMSO-d_6, δ ppm): δ 19.8, 125.0, 125.4, 125.6, 127.2, 127.4, 128.3, 128.5, 129.2, 131.2, 136.1, 136.2, 137.4, 142.2, 145.3, 162.0; MS (m/z): 345 (M+H); Anal. Calcd for $C_{16}H_{12}N_{10}$: C: 55.81.; H: 3.51.; N: 40.68. Found: C: 55.72.; H: 3.44.; N: 40.60.

***N*-[5-(2-nitrophenyl)-*1H*-tetrazol-1-yl]tetrazolo*[1,5-a]*quinoxalin-4yl-amine (4c):**



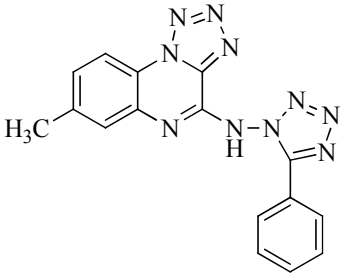
Yield: 61%; m. p: 267- 269 ^oC; IR (KBr, cm^{-1}): 1542 (C-N), 1661 (C=N), 3435(-NH); ^{1}HNMR (400MHz, DMSO-d_6, δ ppm): δ 7.20-7.30 (m, 4H, Ar-H), 7.50-7.88 (m, 4H. Ar-H). 11.40 (bs, 1H, -NH); ^{13}CNMR (100MHz, DMSO-d_6, δ ppm): δ 121.3, 125.0, 125.9, 127.8, 128.2, 128.4, 129.8, 131.5, 135.2, 135.4, 140.1, 141.2, 142.5, 148.2, 162.5; MS (m/z): 376 (M+H); Anal. Calcd for $C_{15}H_9N_{11}O_2$: C: 48.00.; H: 2.42.; N: 41.05. Found: C: 48.00.; H: 2.45.; N: 41.03.

***N*-[5-(3-nitrophenyl)-*1H*-tetrazol-1-yl]tetrazolo*[1,5-a]*quinoxalin-4yl-amine (4d):**



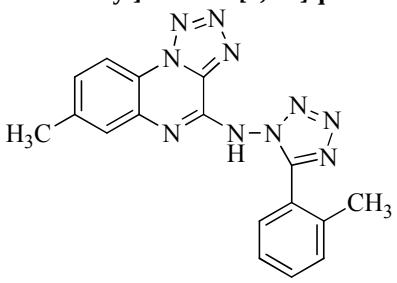
Yield: 59%; m.p: 288-290 ^oC; IR (KBr, cm^{-1}): 1548 (C-N), 1667 (C=N), 3438 (-NH); ^{1}HNMR (400MHz, DMSO-d_6, δ ppm): δ 7.20-7.30 (t, 1H, Ar-H), 7.40-7.60 (m, 4H, Ar-H), 7.70 (s, 1H, Ar-H), 7.82-7.88 (dd, 1H, Ar-H), 8.18 (d, 1H, Ar-H), 11.60 (s, 1H, -NH); ^{13}CNMR (100MHz, DMSO-d_6, δ ppm): δ 122.5, 126.4, 127.8, 128.3, 129.3, 130.2, 131.4, 133.5, 135.2, 135.9, 137.2, 142.1, 148.3, 161.0, 162.8; MS (m/z): 376 (M+H); Anal. Calcd for $C_{15}H_9N_{11}O_2$: C: 48.02.; H: 2.42.; N: 41.05. Found: C: 47.92.; H: 2.40.; N: 41.10.

7-methyl-*N*-(5-phenyl-1*H*-tetrazol-1-yl)tetrazolo*[1,5-a]*quinoxalin-4-amine (4e):



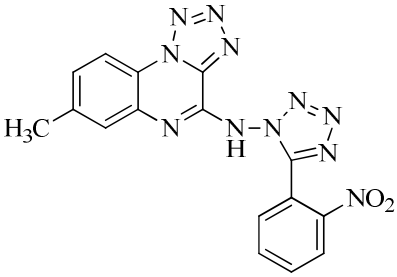
Yield: 71 %; m. p: 252-254 ^{o}C; IR (KBr, cm^{-1}): 1541(C-N), 1625 (C=N), 3410 (-NH). ^{1}HNMR (400MHz, DMSO-d_6, δppm): δ 2.40 (s, 3H, -CH_3) 7.02-7.40 (m, 5H, Ar-H), 7.45-7.58 (d, 1H, Ar-H), 7.60 (d, 1H, Ar-H), 7.80 (s, 1H, Ar-H), 11.22 (s, 1H, -NH); ^{13}C NMR (100MHz, DMSO-d_6, δ ppm): δ 25.3, 125.5, 126.3, 127.0, 127.3, 127.5, 128.1, 129.1, 130.7, 133.2, 134.8, 137.2, 142.0, 159.3, 161.2, 163.3; MS (m/z): 345 (M+H); Anal. Calcd for $C_{16}H_{12}N_{10}$: C: 55.80.; H: 3.51.; N: 40.68. Found: C: 55.77.; H: 3.47.; N: 40.64.

7-methyl-*N*-[5-(2-methylphenyl)-1*H*-tetrazol-1-yl]tetrazolo*[1,5-a]*quinoxalin-4yl-amine (4f):



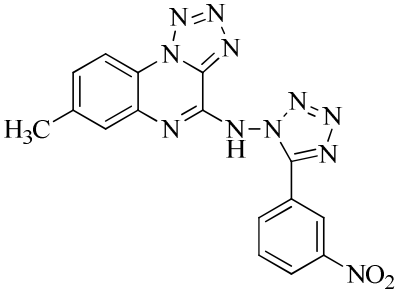
Yield: 74%; m. p: IR (KBr, cm^{-1}): 1545 (C-N), 1632 (C=N), 3400 (-NH); ^{1}HNMR (400MHz, DMSO-d_6, δ ppm): δ 2.60 (s, 3H, -CH_3), 2.68 (s, 3H, -CH_3), 7.18-7.38 (m, 4H, Ar-H), 7.65 (d, 1H, Ar-H), 7.82 (d, 1H, Ar-H), 7.92 (s, 1H, Ar-H), 11.24 (br, s, 1H, -NH); ^{13}CNMR (100MHz, DMSO-d_6, δ ppm): δ 19.5, 21.5, 126.3, 126.5, 127.8, 128.2, 127.8, 129.4, 130.8, 134.8, 136.8, 135.8, 138.8, 140.2, 142.5, 143.5, 163.6; MS (m/z): 358 (M+H); Anal.Calcd for $C_{17}H_{14}N_{10}$: C: 56.98.; H: 3.91.; N: 39.09. Found: C: 56.92; H: 3.87; N: 39.04.

N-[5-(2-nitrophenyl)-1*H*-tetrazol-1-yl]-7-methyltetrazolo*[1,5-a]*quinoxalin-4yl-amine (4g):



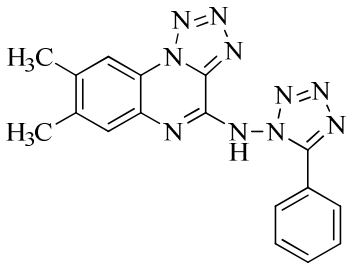
Yield: 67 %; m. p: 298-300 ^{o}C; IR (KBr, cm^{-1}): 1537 (C-N), 1664 (C=N), 3425 (-NH); ^{1}HNMR (400MHz, DMSO-d_6, δ ppm): δ 2.15 (s, 3H, -CH_3), 7.47-7.52 (m, 4H, Ar-H), 7.80-7.82 (d, 1H, Ar-H), 7.88-7.92 (d, 1H, Ar-H), 7.98-8.10 (s, 1H, Ar-H), 11.80 (br, s, 1H, -NH); ^{13}CNMR (100MHz, DMSO-d_6, δ ppm): δ 21.1, 122.4, 126.6, 127.2, 127.4, 129.4, 130.4, 132.6, 134.8, 135.4, 135.8, 136.2, 136.5, 143.8, 149.9, 163.3; MS (m/z): 389 (M+H); Anal. Calcd for $C_{16}H_{11}N_{11}O_2$: C: 49.36.; H: 2.85.; N: 39.57. Found: C: 49.37.; H: 2.83.; N: 39.54.

7-Methyl-*N*-[5-(3-nitrophenyl)-*1H*-tetrazol-1-yl]tetrazolo*[1,5-a]*quinoxalin-4-amine (4h):



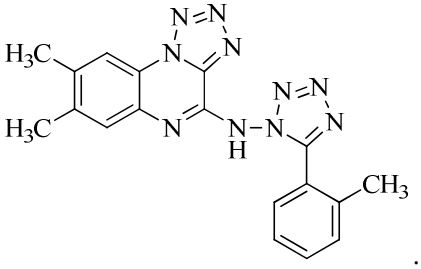
Yield: 54%; m.p: 347-349 ^{o}C; IR (KBr, cm^{-1}): 1564 (C-N), 1672 (C=N), 3463 (-NH); ^{1}HNMR (400MHz, DMSO-d$_6$, δppm): δ 2.32 (s, 3H, CH_3), 7.16-7.21 (t, 1H, Ar-H), 7.48 (d, 1H, Ar-H), 7.85 (d, 1H, Ar-H), 7.92 (s, 1H, Ar-H), 7.96 (d, 1H, Ar-H), 8.22 (d, 1H, Ar-H), 8.42 (s, 1H, Ar-H), 11.65 (br, s, 1H, -NH); ^{13}CNMR (100MHz, DMSO-d$_6$, δ ppm): δ 23.6, 123.6, 126.5, 128.3, 128.9, 130.2, 131.2, 133.5, 134.5, 136.2, 136.9, 141.0, 143.0, 149.2, 162.1, 163.9; MS (m/z): 390 (M+H); Anal.Calcd for $C_{16}H_{11}N_{11}O_2$: C: 49.36.; H: 2.85.; N: 39.97. Found: C: 49.30.; H: 2.79.; N: 39.94.

7,8-dimethyl-*N*-(5-phenyl-1*H*-tetrazol-1-yl)tetrazolo[1,5-*a*]quinoxalin-4-amine (4i):



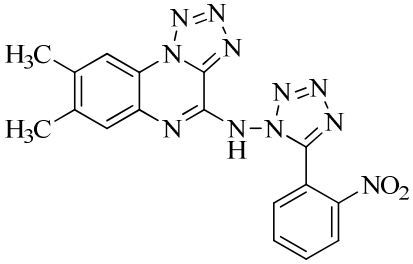
Yield: 58%; m.p:287-289^{o}C; IR (KBr, cm^{-1}): 1547 (C-N), 1632 (C=N), 3345 (-NH); ^{1}HNMR (400MHz, DMSO-d$_6$, δ ppm): δ 2.35 (s, 3H, -CH_3), 2.38 (s, 3H, -CH_3), 7.65 (s, 1H, Ar-H), 7.72 (s, 1H, Ar-H), 7.82-8.28 (m, 5H, Ar-H), 11.02 (br, s, 1H, -NH); ^{13}CNMR (100 MHz, DMSO-d$_6$, δ ppm): δ 21.2, 22.1, 124.6, 125.2, 127.2, 127.5, 127.9, 130.7, 131.2, 133.7, 134.6, 139.2, 140.2, 143.5, 147.2, 160.2, 163.5; MS (m/z): 360 (M+H); Anal. Calcd for $C_{17}H_{14}N_{10}$: C: 56.98.; H: 3.94.; N: 39.09: Found: C: 56.94.; H: 3.90.; N: 39.03.

7,8-dimethyl-*N*-[5-(2-methylphenyl)-1*H*-tetrazol-1-yl]tetrazolo[1,5-*a*]quinoxalin-4-amine (4j):



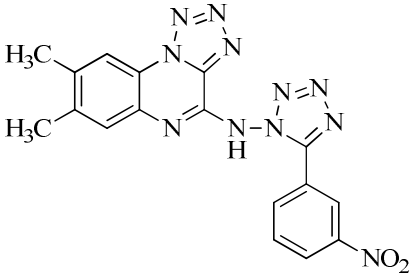
Yield: 61 %; m.p: 278-280^{o}C; IR (KBr, cm^{-1}): 1518 (C-N), 1608 (C=N), 3408 (-NH); ^{1}HNMR (400MHz, DMSO-d$_6$, δ ppm): δ 2.42 (s, 3H, -CH_3), 2.55 (s, 3H, -CH_3), 2.65 (s, 3H, CH_3), 7.45-7.56 (m, 4H, Ar-H), 7.85 (s, 1H, Ar-H), 7.92 (s, 1H, Ar-H), 11.15 (br, s, 1H, -NH); ^{13}CNMR (100MHz, DMSO-d$_6$, δ ppm): δ 19.2, 21.4, 22.9, 124.6, 126.4, 128.6, 129.2, 129.5, 130.4, 133.5, 134.2, 136.5, 138.2, 140.1, 143.2, 147.2, 160.8, 163.1; MS (m/z): 373 (M+H). Anal. Calcd for $C_{18}H_{16}N_{10}$: C: 58.06.; H: 4.33.; N: 37.61. Found: C: 58.02.; H: 4.32.; N: 37.59.

7,8-dimethyl-*N*-[5-(2-nitrophenyl)-1*H*-tetrazol-1-yl]tetrazolo[1,5-*a*]quinoxalin-4-amine (4k):



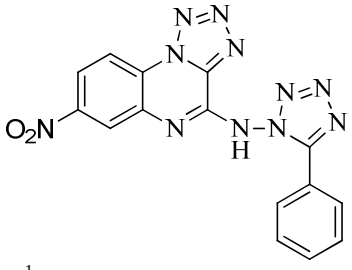
Yield: 65 %; m.p: 312-314^{o}C; IR (KBr, cm^{-1}): 1522 (C-N), 1622 (C=N), 3432 (-NH); ^{1}HNMR (400MHz, DMSO-d_6, δ ppm): δ 2.71(s, 3H, -CH_3), 2.78 (s, 3H, -CH_3), 7.70 (s, 1H, Ar-H), 7.79 (s, 1H, Ar-H), 7.68-8.10 (m, 4H, Ar-H), 11.65 (br, s, 1H, -NH); ^{13}CNMR (100MHz, DMSO-d_6, δ ppm): δ 21.5, 22.5, 124.5, 124.8, 126.2,126.8, 129.7, 132.2, 133.7, 134.5, 135.7, 139.2, 143.5, 147.6, 150.2, 189.4, 164.5; MS (m/z): 404 (M+H); Anal. Calcd for $C_{17}H_{13}N_{11}O_2$: C: 50.62.; H: 3.52.; N: 38.20. Found: C: 50.58.; H: 3.49.; N: 38.18.

7,8-dimethyl-*N*-[5-(3-nitrophenyl)-1*H*-tetrazol-1-yl]tetrazolo[1,5-*a*]quinoxalin-4-amine (4l):



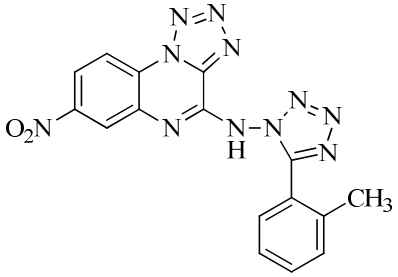
Yield: 55%; m.p: 341-343^{o}C; IR (KBr, cm^{-1}): 1545 (C-N), 1668 (C=N), 3466 (-NH); ^{1}HNMR (400MHz, DMSO-d_6,δ ppm): δ 2.56 (s, 3H, -CH_3), 2.71 (s, 3H, -CH_3), 7.82 (s, 1H, Ar-H), 7.88 (s, 1H, Ar-H), 8.05 (t, 1H, Ar-H), 8.17 (d, 1H, Ar-H), 8.20 (d, 1H, Ar-H), 8.21 (s, 1H, Ar-H), 11.68 (br, s, 1H, -NH); ^{13}CNMR (100MHz, DMSO-d_6, δ ppm): δ 22.4, 23.7, 122.7, 123.9, 124.7, 126.6, 130.1, 131.4, 133.6, 133.9, 134.6, 140.2, 143.5, 147.2, 148.4, 161.2, 163.9; MS (m/z): 404 (M+H).Anal. Calcd for $C_{17}H_{13}N_{11}O_2$: C, 50.62.; H, 3.25.; N, 38.20. Found: C, 50.59.; H, 3.24.; N, 38.18.

7-nitro-*N*-(5-phenyl-1*H*-tetrazol-1-yl)tetrazolo[1,5-*a*]quinoxalin-4-amine (4m):



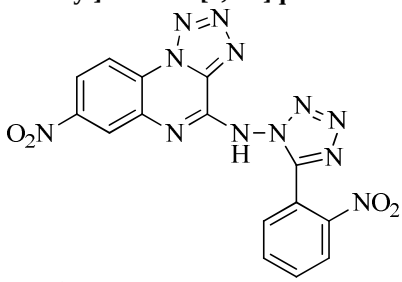
Yield: 53 %; m.p: 361-363^{o}C; IR (KBr, cm^{-1}): 1532 (C-N), 1632 (C=N), 3396 (-NH); ^{1}HNMR (400MHz, DMSO-d_6, δ ppm): δ 7.36-7.45 (m, 5H, Ar-H), 7.85 (d, 1H, Ar-H), 7.98 (d, 1H, Ar-H), 8.24 (s, 1H, Ar-H), 11.25 (br, s, 1H, -NH); ^{13}CNMR (100MHz, DMSO-d_6, δ ppm): δ 118.6, 119.2, 127.5, 127.8, 129.2, 129.6, 129.8, 130.7, 131.5, 138.2, 139.2, 140.2, 141.5, 163.7, 164.2; MS (m/z): 376 (M+H); Anal.Calcd for $C_{15}H_9N_{11}O_2$: C: 48.00.; H: 2.42.; N: 41.05. Found: C: 47.97.; H: 2.39.; N: 41.00.

7-nitro-*N*-[5-(2-methylphenyl)-1*H*-tetrazol-1-yl]tetrazolo[1,5-*a*]quinoxalin-4-amine (4n):



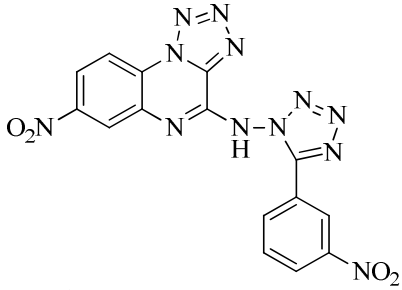
Yield: 56 %; m.p: 378-380^{o}C; IR (KBr, cm^{-1}): 1516 (C-N), 1612 (C=N), 3386 (-NH); ^{1}HNMR (400MHz, DMSO-d$_6$, δ ppm): δ 2.26 (s, 3H, -CH$_3$), 7.35-7.42 (m, 4H, Ar-H). 7.82 (d, 1H, Ar-H), 7.93 (d, 1H, Ar-H), 8.15 (s, 1H, Ar-H), 11.26 (br, s, 1H, -NH); ^{13}CNMR (100MHz, DMSO-d$_6$, δ ppm): δ 23.6, 116.3, 127.5, 128.3, 128.9, 131.2, 131.6, 132.2, 134.5, 136.9, 137.8, 138.2, 139.3, 140.3, 161.1, 162.0; MS (m/z): 424 (M+H). Anal. Calcd for $C_{16}H_{11}N_{11}O_2$: C: 49.36.; H: 2.85.; N: 39.57. Found: C: 49.34.; H: 2.82.; N: 39.55.

7-nitro-*N*-[5-(2-nitrophenyl)-1*H*-tetrazol-1-yl]tetrazolo[1,5-*a*]quinoxalin-4-amine (4o):



Yield: 51%; m.p: 356-357^{o}C; IR (KBr, cm^{-1}): 1523 (C-N), 1615 (C=N), 3385 (-NH); ^{1}HNMR (400MHz, DMSO-d$_6$, δ ppm): δ 7.28-7.36 (m, 4H, Ar-H), 7.82 (d, 1H, Ar-H), 7.95 (d, 1H, Ar-H), 8.25 (s, 1H, Ar-H), 11.32 (br, s, 1H, -NH); ^{13}CNMR (100MHz, DMSO-d$_6$, δ ppm): δ 117.2, 119.3, 124.1, 126.3, 129.2, 129.7, 133.5, 135.2, 138.5, 139.2, 140.2, 141.5, 149.7, 163.2, 163.8; MS (m/z): 421 (M+H); Anal. Calcd for $C_{15}H_8N_{12}O_4$: C: 42.80.; H: 1.92.; N: 39.99; Found: C: 42.78.; H: 1.88.; N: 39.98.

7-nitro-*N*-[5-(3-nitrophenyl)-1*H*-tetrazol-1-yl]tetrazolo[1,5-*a*]quinoxalin-4-amine (4p):



Yield: 47%; m. p: 352-354 ^{o}C; IR (KBr, cm^{-1}): 1538 (C-N), 1652 (C=N), 3378 (-NH); ^{1}HNMR (400MHz, DMSO-d$_6$, δ ppm): δ 7.83 (t, 1H, Ar-H), 7.86 (d, 1H, Ar-H), 7.93 (d, 1H, Ar-H), 8.05 (d, 1H, Ar-H), 8.10 (d, 1H, Ar-H), 8.18 (s, 1H, Ar-H), 8.35 (s, 1H, Ar-H), 11.56 (br, s, 1H, -NH); ^{13}CNMR (100MHz, DMSO-d$_6$, δ ppm): δ 117.8, 119.2, 122.5 123.4, 129.5, 130.2, 131.2, 133.6, 138.4, 139.5, 140.2, 141.2, 148.5, 164.7, 165.4; MS (m/z): 421 (M+H); Anal. Calcd for $C_{15}H_8N_{12}O_4$: C: 42.80.; H: 1.92.; N: 39.99. Found: C: 42.77.; H: 1.85.; N: 33.97.

Anti-microbial activity:

The newly synthesized compounds **4(a-p)** were screened for in vitro anti-bacterial and anti-fungal activity against various Gram positive bacteria S.*aures* and Gram negative bacteria E.*Coli* and anti-fungal activity carried out on C.*albicans*, A. *niger*. The agar Disc-diffusion method was used to evaluate anti-microbial activity. The compounds were dissolved in DMSO to 10 µg/mL and 20 µg/mL concentration solutions used. The compounds were placed aseptically on Muller-Hinton Agar for the both Gram positive and Gram negative bacteria and Saboround dextrose agar for fungi and incubated for 24 h at 37^{o}C. At the end of the incubation period, the diameter of the growth of

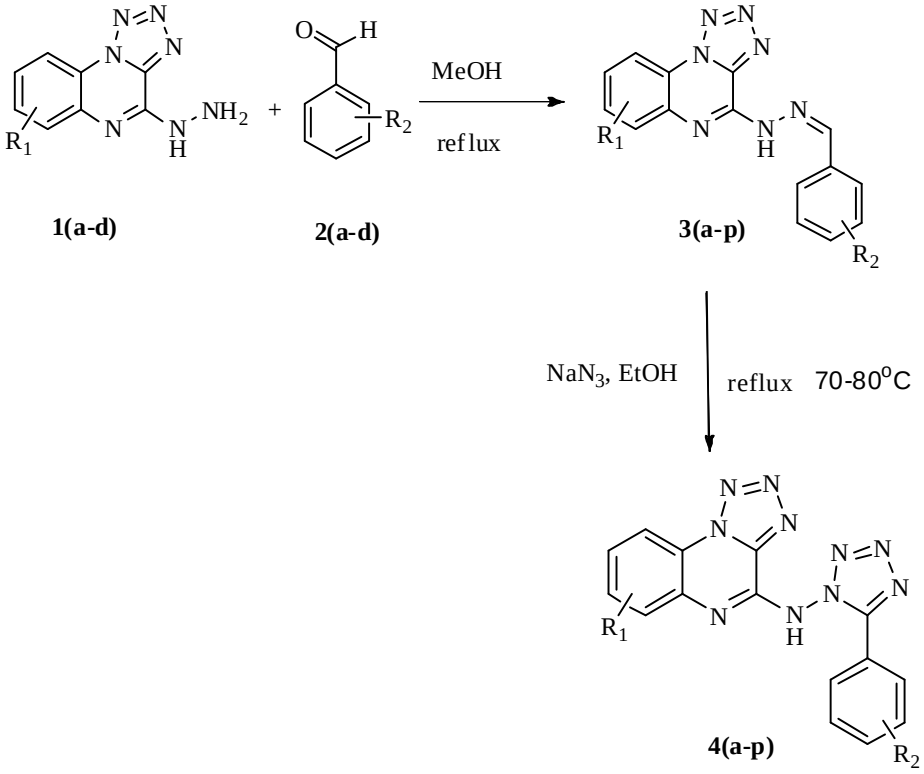
inhibition zones was measured. Two Gram positive bacteria *S. aureus* and Gram negative bacteria *E.coli* were used in the test method. **Ciprofloxacin** was used as the reference compound during the screening of anti-bacterial activity. *C.albicans and A.niger* was used in the test and **Flucanazole** was used as reference standard during the screening of anti-fungal activity.

RESULTS AND DISCUSSION

Chemistry

The preparation of substituted of N-(substituted phenyl-*1H*-tetrazol-1-yl)-7-substituted tetrazolo*[1,5-a]*quinoxalin-4yl-amines **IV-2.2(a-p)** have been carried out by synthetic sequence illustrated in **Scheme**. The starting compound 4-hydrazinyl tetrazolo*[1,5-a]*-quinoxaline **1(a-d)** were prepared according to the reported procedure. The compounds **1(a-d)** were treated with different substituted aromatic aldehydes **2(a-d)** resulted in the formation of corresponding Schiff's base compounds[15] **3(a-p).** The synthesized scaffold were again refluxed with sodium azide in ethanol as solvent to furnished the corresponding substituted *N*-(5-substitutedphenyl)-1*H*-[1,2,3,4-tetrazol-1-yl]-*N*-*[1,2,3,4]* tetrazolo*[1,-5a]*-quinoxalin-4-yl-amine **4(a-p)** in good yields. The yields of all the synthesized compounds were found to be in the range of 78-86%. The structures of the all newly synthesized compounds were characterized on the basis of elemental analysis, IR, ^{1}H NMR, ^{13}C NMR and Mass spectral data. The synthesized compounds were also screened for their anti-microbial activity.

Scheme



1(a-d) **2(a-d)** **3(a-p)** **4(a-p)**

Table-1

S.No	Compd	R_1	R_2	R_3
1.	a	-H	-H	-H
2.	b	-H	-H	$-CH_3$
3.	c	-H	-H	$2-NO_2$
4.	d	-H	-H	$3-NO_2$
5.	e	$-CH_3$	-H	-H
6.	f	$-CH_3$	-H	$-CH_3$
7.	g	$-CH_3$	-H	$2-NO_2$
8.	h	$-CH_3$	-H	$3-NO_2$
9.	i	$-CH_3$	$-CH_3$	-H
10.	j	$-CH_3$	$-CH_3$	$-CH_3$
11.	k	$-CH_3$	$-CH_3$	$2-NO_2$
12.	l	$-CH_3$	$-CH_3$	$3-NO_2$
13.	m	$-NO_2$	-H	-H
14.	n	$-NO_2$	-H	$-CH_3$
15.	o	$-NO_2$	-H	$2-NO_2$
16.	p	$-NO_2$	-H	$2-NO_2$

Table: 2. Anti-microbial activity result of substituted Substituted *N*-tetrazolo quinoxalino*[1,5-a]* tetrazoles analogues at 10 and 20µg/mL

S.No	Compds.	Concent. µg/ml	Anti-bacterial		Anti-fungal	
			Zone of inhibition in mm			
			S.*aures*	E.*Coli*	C.*albicans*	A. *niger*
1.	4a	10	01	01	-	-
		20	02	01	-	-
2.	4b	10	06	04	-	-
		20	14	08	-	-
3.	4c	10	08	06	-	-
		20	10	07	-	-
4.	4d	10	03	01	-	-
		20	03	02	-	-
5.	4e	10	07	05	02	03
		20	12	10	04	05
6.	4f	10	09	08	04	04
		20	17	18	06	08
7.	4g	10	10	11	04	04
		20	15	17	06	04
8.	4h	10	06	04	-	-
		20	09	07	-	-
9.	4i	10	06	03	-	-
		20	07	05	-	-
10.	4j	10	07	06	01	-
		20	12	10	02	-
11.	4k	10	04	02	-	-
		20	04	02	-	-
12.	4l	10	02	-	-	-
		20	03	01	-	-
13.	4m	10	05	02	-	-
		20	09	04	-	-
14.	4n	10	08	09	02	02
		20	15	14	05	02
15.	4o	10	08	07	01	-
		20	14	12	02	-
16.	4p	10	05	03	-	-
		20	07	03	-	-
	Ciprofloxan	5	20	22	-	-
	Flucanazole	5	-	-	12	10

Biological Activity:

The synthesized compounds were screened for antimicrobial activity by zone of inhibition method. These activity results (**Table: 2)** reveals that some of the synthesized compounds **4b, 4g**, **4n** and **4o** showed potent activity against gram positive bacterial strains and gram negative strains S.*aures and* E.*Coli* on comparing with the standard drugs Ciprofloxan. Compound **4c,4e** and **4f** showed a moderate activity against tested bacterial strains. The anti-fungal screening data revealed that all the tested compounds showed moderate to good activity against tested strains. The

highest zone of inhibition was recorded against *Candida Albicans* and *Aspergillus niger* towards compound **4f** and remaining compounds **4e, 4g** and **4n** showed moderate activity against *Candida Albicans* and *Aspergillus niger*

CONCLUSION

We have synthesized new *N*-(substitutedphenyl-*1H*-tetrazol-1-yl)-7-substituted tetrazolo*[1,5-a]*quinoxalin-4yl-amine derivatives 4(a-p) by treating 4-hydrazinyl tetra- zolo quinoxalines with substituted aromatic aldehydes in ethanol. All the synthesized compounds **4(a-p)** were screened for anti-microbial activity. Among all the synthesized compounds **4b, 4g**, **4n** and **4o** are showed good activity and **4c, 4e** and **4f** exhibited moderate activity against gram-positive bacterial strains *S. aureus* and gram-negative bacterial strains *E.coli*. **4f** showed good activity and compounds **4e, 4g** and **4n** showed moderate activity against *C. Albicans* and *A. niger*.

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